

AMENDMENTS TO THE CLAIMS

1. **(Currently Amended)** A method for identifying a compound that induces a morphogen-mediated biological effect, the morphogen selected from OP-1, OP-2, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-9, Vgl, Vgr-1, DPP, or 60A, the method comprising:
 - (a) providing a test cell comprising a DNA comprising:
 - (i) a transcription activating element that is responsive to, and distinct from the gene encoding, said morphogen, and
 - (ii) a reporter gene encoding a detectable gene product, the transcription activation element being in operative association with the reporter gene, wherein the reporter gene is transcribed when the DNA is present in a cell that is
 - (1) responsive to the morphogen, and
 - (2) contacted with said morphogen;
 - (b) exposing said test cell to a candidate compound; and
 - (c) detecting expression of said detectable gene product, wherein an increase in expression of said detectable gene product after exposing said test cell to said candidate compound indicates the ability of the compound to induce the morphogen-mediated biological effect;wherein said morphogen-mediated biological effect requires the presence of said morphogen-responsive transcription activating element, so as to thereby identify a compound that induces a biological effect mediated by a morphogen.
2. **(Original)** The method of claim 1 wherein said morphogen responsive transcription activating element binds with a protein having general DNA-binding properties of a MEF-2 family protein, said DNA binding inducible by performing step (b).
3. **(Previously Presented)** The method of claim 1, wherein said morphogen responsive transcription activating element comprises a sequence that hybridizes to an MEF-2 binding site sequence.

4. **(Previously Presented)** The method of claim 1 wherein said morphogen responsive transcription activating element comprises nucleotides 699-731 of SEQ ID NO: 1.
5. **(Previously Presented)** The method of claim 1 wherein said morphogen responsive transcription activating element comprises nucleotides 682-761 of SEQ ID NO: 1.
6. **(Original)** The method of claim 1 wherein said morphogen responsive transcription activating element comprises a sequence of A and T residues.
7. **(Previously Presented)** The method of claim 6 wherein the sequence of A and T residues comprises nucleotides 699-711 of SEQ ID NO: 1.
8. **(Previously Presented)** The method of claim 6 wherein the sequence of A and T residues comprises nucleotides 703-724 of SEQ ID NO: 1.
9. **(Original)** The method of claim 6 wherein the A and T residues are adjacent to an AP-1 binding site sequence.
10. **(Previously Presented)** The method of claim 9 wherein the AP-1 binding site sequence comprises nucleotides 715-724 of SEQ ID NO: 1, or the nucleotide sequence of SEQ ID NO: 2.
- 11-12. **(Canceled)**
13. **(Previously Presented)** A method of producing a compound competent to induce a biological effect mediated by a morphogen selected from OP-1, OP-2, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-9, Vg1, Vgr-1, DPP, or 60A, the method comprising:
 - a. obtaining said compound by screening at least one candidate compound according to the method of claim 1 or 2; and

- b. producing said compound or a derivative thereof having substantially the same ability as said compound to induce said morphogen mediated biological effect.
14. **(Canceled)**
15. **(Previously Presented)** A method of assessing whether a sample comprises a substance competent to bind to DNA, the sequence of which comprises nucleotides 699-731 of SEQ ID NO: 1, the method comprising:
- a. providing DNA, the sequence of which comprises nucleotides 699-731 of SEQ ID NO: 1;
 - b. exposing said DNA to said sample; and,
 - c. detecting the binding of said substance to said DNA.
- 16-29. **(Canceled)**
30. **(Previously Presented)** A method of detecting a biological effect mediated by a morphogen selected from OP-1, OP-2, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-9, Vg1, Vgr-1, DPP, or 60A, the method comprising detecting DNA binding of a protein that induces said morphogen-mediated biological effect, said protein having a polypeptide sequence of a morphogen-inducible DNA binding protein which can interact with nucleotides 699-711, 715-724, 699-731, 682-731, 703-724 or 682-761 of SEQ ID NO: 1.
31. **(Previously Presented)** The method of claim 30 comprising the additional step of providing said morphogen or analog thereof to a morphogen responsive cell prior to said detecting step, and wherein said DNA binding is detected within about 2 to 12 hours.
32. **(Previously Presented)** The method of claim 30 comprising the additional step of providing said morphogen or analog thereof to a morphogen responsive cell prior to said detecting step, and wherein said DNA binding is detected within about 2 to 6 hours.

33. **(Original)** The method of claim 1, 2, 15 or 30 comprising part of a medium or high-flux screening assay.

34-35. **(Canceled)**

36. **(Currently Amended)** A method for identifying a candidate compound that induces a biological effect mediated by a morphogen selected from OP-1, OP-2, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-9, Vg1, Vgr-1, DPP, or 60A, the method comprising:

- (a) providing a test cell comprising DNA, said DNA comprising a defining a transcription activating element that is responsive to, and distinct from the gene encoding, said morphogen, said DNA, when present in a cell responsive to said morphogen and contacted with said morphogen, serving to induce transcription of a gene operatively associated with said transcription activating element;
- (b) exposing said test cell to a candidate compound; and
- (c) detecting morphogen inducible DNA binding to said transcription activating element by a cellular protein, wherein an increase in said binding after exposing said test cell to said candidate compound indicates the ability of said candidate compound to induce said morphogen mediated biological effect,

wherein step (c) occurs within approximately 2-12 hours of completing step (b), and wherein said morphogen-mediated biological effect requires the presence of said morphogen-responsive transcription activating element.

37-42. **(Canceled)**

43. **(Previously Presented)** The method of claim 1 wherein the morphogen is OP-1.

44. **(Previously Presented)** The method of claim 2, wherein said morphogen-responsive transcription activating element also binds with a second protein having general DNA-binding properties of an AP-1 family protein.

45. **(Previously Presented)** The method of claim 1, wherein the morphogen is OP-2, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, Vg1, Vgr-1, DPP, or 60A.
46. **(Previously Presented)** The method of claim 43 or 45, wherein the morphogen is of human origin.
47. **(Previously Presented)** The method of claim 1, wherein said morphogen-mediated biological effect is: stimulating proliferation of mammalian bone / cartilage progenitor cells, stimulating differentiation of mammalian bone / cartilage progenitor cells, supporting growth and maintenance of mammalian endochondrial bone tissue, delaying or mitigating the onset of senescence or quiescence-associated loss of phenotype or tissue function, stimulating phenotypic expression of differentiated cells, inducing redifferentiation of transformed cells, induction of VEGF expression, induction of PTH-mediated cAMP production in osteoblast, or induction of neuronal marker.
48. **(Previously Presented)** The method of claim 47, wherein said neuronal marker is β -L1 or N-CAM.
49. **(Previously Presented)** The method of claim 1, wherein said morphogen-mediated biological effect is induction of mitogenesis and phenotypic markers for chondrocyte or osteoblast differentiation.
50. **(Previously Presented)** The method of claim 49, wherein said phenotypic markers is: type I collagen, type II collagen, type X collagen, alkaline phosphatase, osteocalcin, N-cadherin, N-CAM, or MSX-2.